Food and Drug Interactions with Urine Drug Tests

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Objectives
- Methods of urine drug testing (UDT)
- Drug-class specific windows of detection
- Metabolism of opiates and how it affects UDT
- Drug and food that can cause false positive UDT
- UDT clinical pearls

Background
- UDT is a common feature of clinic opioid contracts
- UDT typically detects parent drugs and/or their metabolites with a 1 to 3 day window of detection
- Initial testing is often done in clinic with class-specific immunoassays
- Definitive identification is done in the laboratory with gas chromatography-mass spectrometry (GC/MS), high performance liquid chromatography (HPLC), or liquid chromatography-mass spectrometry (LC/MS)

Why Test?
- To assist in the diagnosis of substance misuse or addiction
- To support treatment decisions made in urgent care settings
- To assist in monitoring adherence to a controlled substance treatment regimen

Algorithm for UDT in Chronic Pain

Pop Quiz: True or False?
- Urine samples have longer drug detection time than blood samples?
- Oxycodone can be detected by most opiate screening immunoassays?
- Passive smoke inhalation of marijuana can result in positive marijuana test?
- Use of tramadol can result in positive opiate test?
Relative Detection Times of Drugs in Biologic Specimens

Approximate Windows of Detection of Drugs in the Urine

<table>
<thead>
<tr>
<th>Drug</th>
<th>Detection time in urine</th>
</tr>
</thead>
<tbody>
<tr>
<td>Amphetamines</td>
<td>Up to 3 days</td>
</tr>
<tr>
<td>THC (depending on the grade and frequency of marijuana use)</td>
<td></td>
</tr>
<tr>
<td>– Single use</td>
<td>1 to 3 days</td>
</tr>
<tr>
<td>– Chronic use</td>
<td>Up to 30 days</td>
</tr>
<tr>
<td>Benzoylegonine after cocaine use</td>
<td>2 to 4 days</td>
</tr>
<tr>
<td>Opiates (morphine, codeine)</td>
<td>2 to 3 days</td>
</tr>
<tr>
<td>Methadone (– EDDP (methadone metabolite))</td>
<td>Up to 3 days</td>
</tr>
<tr>
<td>– EDDP (methadone metabolite)</td>
<td>Up to 6 days</td>
</tr>
<tr>
<td>Benzodiazepines (depending on specific agent and quantity used)</td>
<td>Days to weeks</td>
</tr>
</tbody>
</table>

Methods of UDT

- Laboratory-based specific drug identification
  - More definitive procedure (i.e. GC/MS, LC/MS) to identify specific drugs:
    - Confirm the presence of a given drug (i.e. morphine is the opiate causing the positive opiate immunoassay response)
    - Identify drugs not included in an immunoassay test
    - When results are contested

Initial and Confirmatory Cut-Off Concentrations

<table>
<thead>
<tr>
<th>Test</th>
<th>Initial Test Analyte</th>
<th>Initial Test Cutoff</th>
<th>Confirmatory Test Cutoff</th>
</tr>
</thead>
<tbody>
<tr>
<td>COC</td>
<td>Benzoylglycine</td>
<td>100ng/mL</td>
<td>100ng/mL</td>
</tr>
<tr>
<td>M-AMP</td>
<td>Methamphetamine</td>
<td>1,000ng/mL</td>
<td>1,000ng/mL</td>
</tr>
<tr>
<td>THC</td>
<td>Marijuana metabolites</td>
<td>50ng/mL</td>
<td>50ng/mL</td>
</tr>
<tr>
<td>MTD</td>
<td>Methadone</td>
<td>100ng/mL</td>
<td>100ng/mL</td>
</tr>
<tr>
<td>EUR</td>
<td>Morfina, Codeina</td>
<td>100ng/mL</td>
<td>100ng/mL</td>
</tr>
<tr>
<td>BZO</td>
<td>Oxazepam, Noroxazepam, OH- Aclonazol, Desalicylflurazepam</td>
<td>500ng/mL</td>
<td>500ng/mL</td>
</tr>
<tr>
<td>OXY</td>
<td>Oxycodone</td>
<td>100ng/mL</td>
<td>100ng/mL</td>
</tr>
</tbody>
</table>
Collection of Urine

- Random collection is preferred
- Concentrated urine samples are generally more reliable than dilute samples
- If tampering is suspected check urine temperature, pH, and creatinine:
  - 90 - 100°F
  - pH 4.5 - 8.0
  - Creatinine concentration > 20 mg/dL

Detection of Opiates

<table>
<thead>
<tr>
<th>Opiate</th>
<th>Source of Opiate</th>
<th>Synthetic Opiate</th>
<th>Synthetic Metabolite</th>
</tr>
</thead>
<tbody>
<tr>
<td>Codeine</td>
<td>Plant opium (narcotic)</td>
<td>Synthetic Heroin</td>
<td>Synthetic Morphine</td>
</tr>
<tr>
<td>Morphine</td>
<td>Opioid derived from fungus</td>
<td>Synthetic Hydrocodone</td>
<td>Synthetic Hydromorphone</td>
</tr>
<tr>
<td>Hydromorphone</td>
<td>Synthetic Opioid</td>
<td>Synthetic EDDP</td>
<td>Synthetic Heroin</td>
</tr>
<tr>
<td>MDA</td>
<td>Synthetic Opioid</td>
<td>Synthetic EDDP</td>
<td>Synthetic Heroin</td>
</tr>
</tbody>
</table>

Opiates False (+)

- Poppy seeds
- Rifampin
- Quinolone antibiotics (i.e. levofloxacin, ciprofloxacin, moxifloxacin)
- Dextromethorphan

Methadone

- Synthetic opioid
- Urinary excretion is dependent on urine pH with higher concentration at lower pH
- Excretion of metabolite EDDP is not dependent on urinary pH
- False positive:
  - Quetiapine (Seroquel)
  - Doxylamine (Unisom)
  - Chlorpromazine (Thorazine)

Oxycodone

- Semi-synthetic opiate
- Unable to detect with opiate urine dipstick
- Require oxycodone urine dipstick
- Oxycodone immunoassay
  - (+) in urine with oxycodone concentration cutoff 100ng/mL
  - (+) in urine with high concentration of hydromorphone and hydrocodone

Tetrahydrocannabinol (THC)

- Psychoactive ingredient of marijuana
- False positive:
  - Dronabinol
  - Pantoprazole
  - Hemp seed
  - Efavirenz
Cocaine
- Immunoassay detects cocaine and its primary metabolite benzoylecgonine
- Low cross-reactivity with other substances
- Highly predictive of cocaine use
- Coca leaf tea (+)

Methamphetamine
- Immunoassay is highly cross-reactive
- Ephedrine/pseudoephedrine
- Bupropion
- Desipramine
- Amantadine
- Ranitidine
- Selegiline
- Phenylpropanolamine
- Vicks Vapor Inhaler
- Further testing with more specific methods is recommended if immunoassay is positive for methamphetamine

Benzodiazepine
- Extensively metabolized; only traces of most benzodiazepines are excreted unchanged in the urine
- UDT primarily detects metabolites
- Detection period is ~3-7 days (longer with chronic use)
- False positive:
  - Oxaprozin (Daypro)
  - Sertaline (Zoloft)

Case
- LK is a 59 yo M with chronic hep C, hx of narcotic abuse, currently being prescribed Methadone and Vicodin for chronic shoulder and low back pain
- Current Medications:
  - Vitamin D 2000 units QD
  - Benazepril 10mg QD
  - Vicodin 5-500mg QID prn
  - Methadone 10mg QAM and 15mg QPM

UDT results
- Methadone by GC/MS = 550ng/mL
- Opiates confirmatory GC/MS
  - Codeine = negative
  - Morphine = >15,000ng/mL
  - Hydrocodone = negative
  - Hydromorphone = negative
  - Oxycodone = negative
- EIA 6 w/ Oxycodone
  - Oxycodone = negative
  - Oxymorphone = negative
  - Amphetamine = negative
  - Benzodiazepines = negative
  - Cannabinoid = negative
  - Cocaine = negative

Conclusion
- UDT can be an effective tool in assessing and managing adherence, diversion, and abuse
- Point of care UDT immunoassays are not highly specific and samples should be sent for GC/MS to confirm unexpected or disputed results
- Clinician can utilize discordant UDT result to motivate patient behavior change
- Quick reference:
  - Test Interactions section in LexiDrugs
References

5. One Step Drug Screen Test Card [package insert]. Santa Rosa, CA; Redwood Toxicology Laboratory; 2006.